

INTRODUCTION

Worldwide the prevalence of xerosis increases with advancing age, affecting up to 75% of older people.¹ The development of xerotic conditions, such as atopic dermatitis (AD), asteatotic eczema and winter xerosis, is associated with a skin barrier defect (Figure 1).² This defect is characterized by reduced natural moisturising factor (NMF, comprising sodium pyrrolidone carboxylic acid [PCA], urea and lactic acid etc) and abnormal levels of intercellular lipids (cholesterol, ceramides and free fatty acids) in the stratum corneum (SC).³⁻⁶ As we age the integrity of the skin barrier declines, and recovery following disruption slows, increasing the skins susceptibility to negative environmental factors.⁷

Emollients are widely used to treat xerosis, however there is limited mechanistic evidence of their effects on the skin barrier.

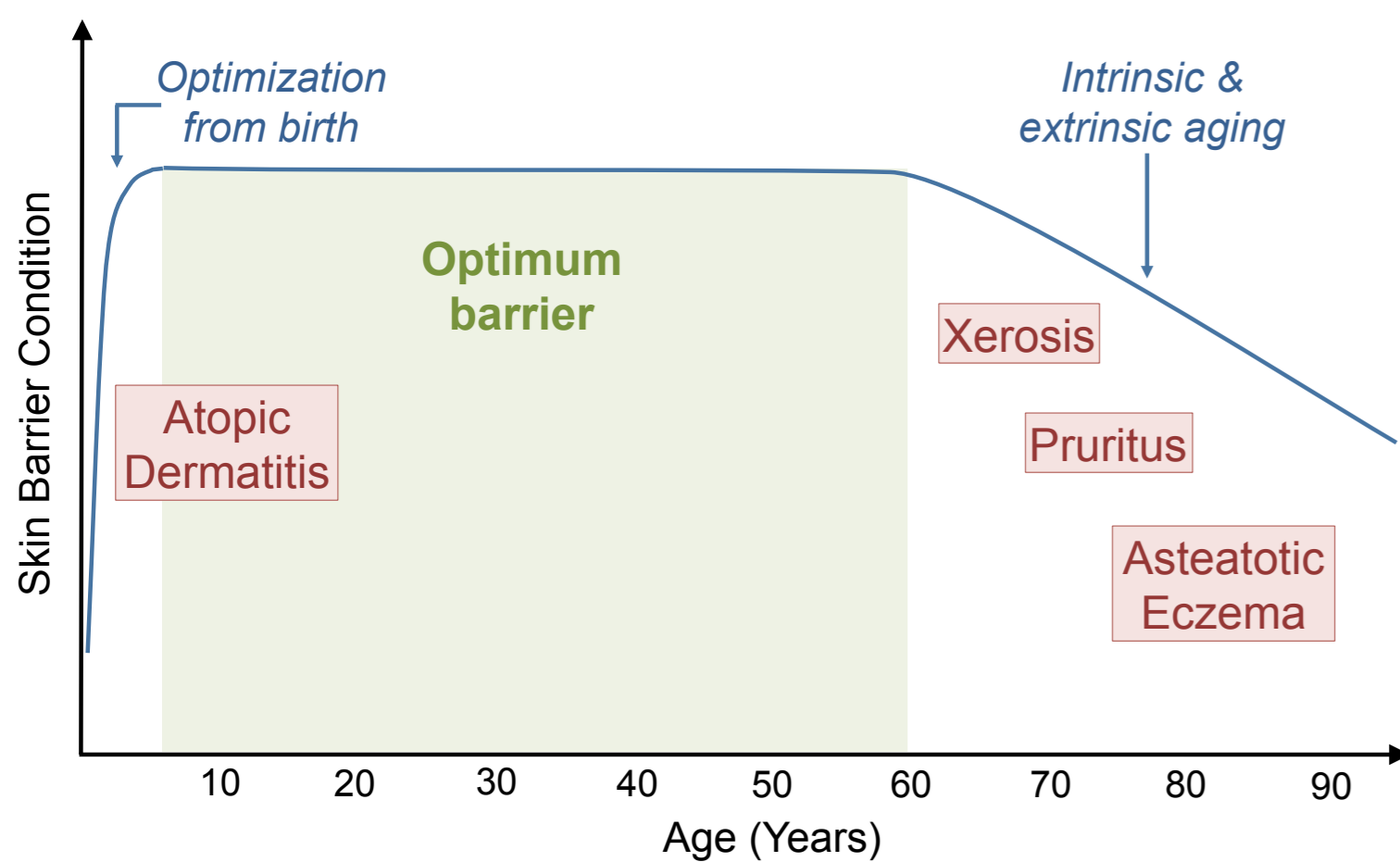


Figure 1: Skin barrier condition changes with age

Aim: To compare the effect of a humectant-emollient to a non-humectant emollient, on the properties of the skin barrier.

METHODS

21 volunteers over the age of 60 with self-reported dry skin were recruited (mean age 68, 14 female), of which 18 completed the study. Each volunteer applied two finger-tip-units (FTU) of humectant emollient (Balneum cream, Almirall-Hermal GmbH) to one forearm and 2 FTU of non-humectant emollient (Aquamol cream, Thornton & Ross Ltd) to the other (allocation randomized) twice daily for 28 days. Before and after (12-20 hours) the treatment period the following assessments were made:

- Skin barrier function was determined by measuring transepidermal water loss (TEWL) using an AquaFlux TEWL machine (Biox, UK)⁸
- SC integrity was determined using tape-stripping in conjunction with TEWL
- Skin surface pH and SC hydration were measured using a Skin-pH-meter and Corneometer respectively (C&K, Germany)
- Caseinolytic protease activity was determined for samples of SC removed by tape-stripping based on a previously published method⁹
- FTIR spectra were collected using a silver halide fibre-optic probe attached to a Nicolet iS50 FTIR spectrometer (Thermo Fisher Scientific Inc), equipped with a cooled MCT detector and purged with dry N₂. 32 scans were collected for each measurement at 4 w/n resolution. Spectral analysis was performed using Omnic 9.0 software (Thermo Electron Corp., Madison, USA).
- The levels of PCA in SC samples collected on tape-strips (strips 4-6 pooled) were quantified as previously described.¹⁰
- Lactate samples were collected using a pre-wetted cotton-swab, and the concentration determined by fluorometric L-Lactate assay (Abcam).

For reference results are presented alongside data collected from the following:

- 5 patients with AD (UK working party diagnostic criteria), all women aged 22-27; SCORAD 35±2. Both forearms assessed without any treatments (use of topical products not permitted for 24 hours prior to assessments).
- 9 volunteers with healthy skin (no history of skin conditions or atopy) aged <60 years.

To assess the effects of the humectant emollient throughout the thickness of the SC the healthy participants detailed above applied 2 FTU to one forearm chosen at random. 3 hours post-application tape-stripping was performed in conjunction with FTIR measurements (as described above) to assess the molecular changes down through the depth of the SC.

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FURTHER INFORMATION

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RESULTS

1. Treatment with the humectant emollient for 28 days preserves normal skin barrier function in older people with dry skin

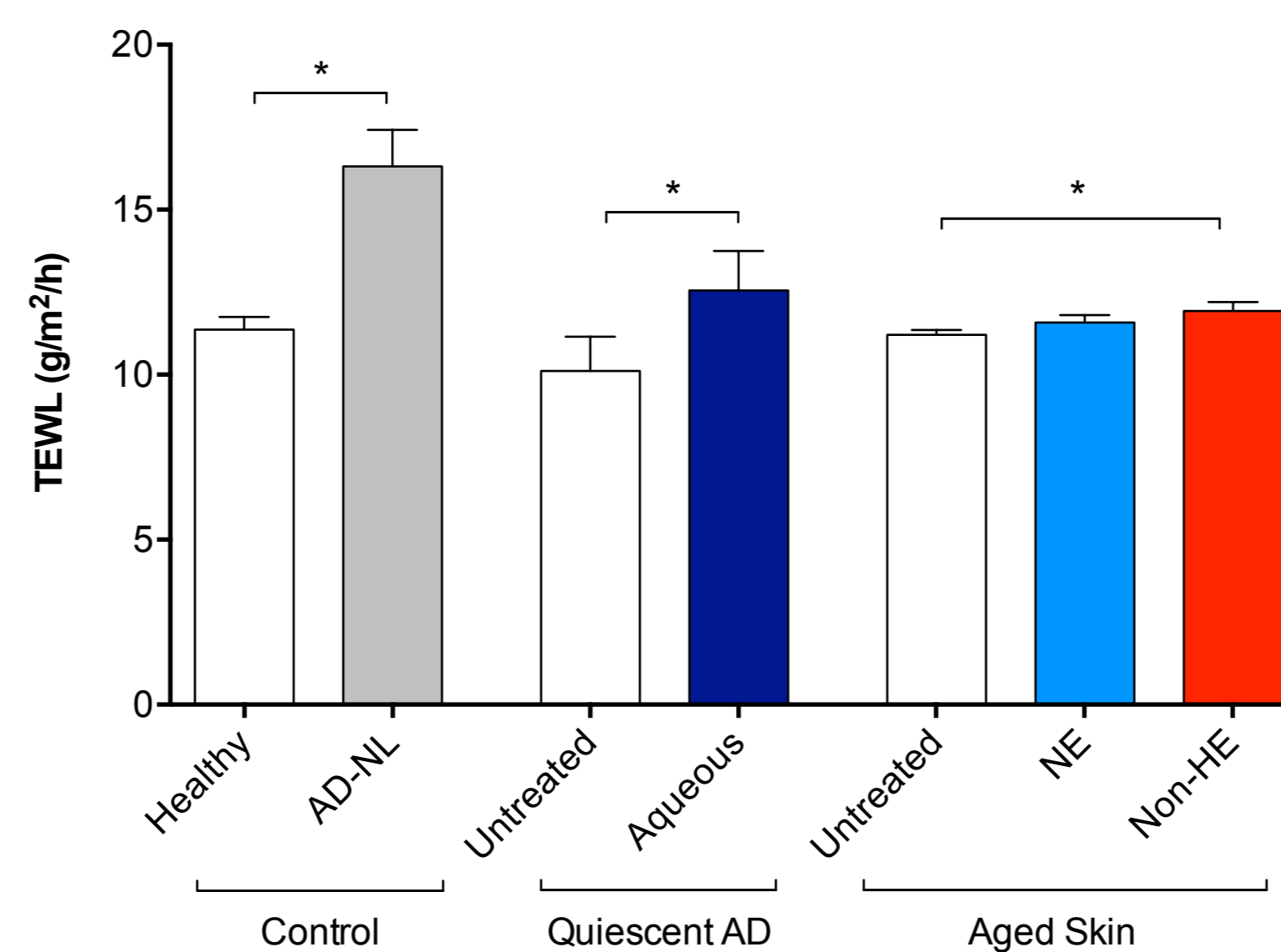


Figure 2: TEWL before and after 28-days treatment with the humectant (HE) and non-humectant (Non-HE) emollients in participants aged over 60 years with dry skin. For comparison TEWL in AD patients at non-lesional sites (AD-NL) and healthy controls and TEWL before and after 28-days treatment with Aqueous cream in participants with quiescent AD is presented.¹¹

2. Treatment with the humectant emollient improved SC integrity compared to untreated skin and skin treated with the non-humectant emollient

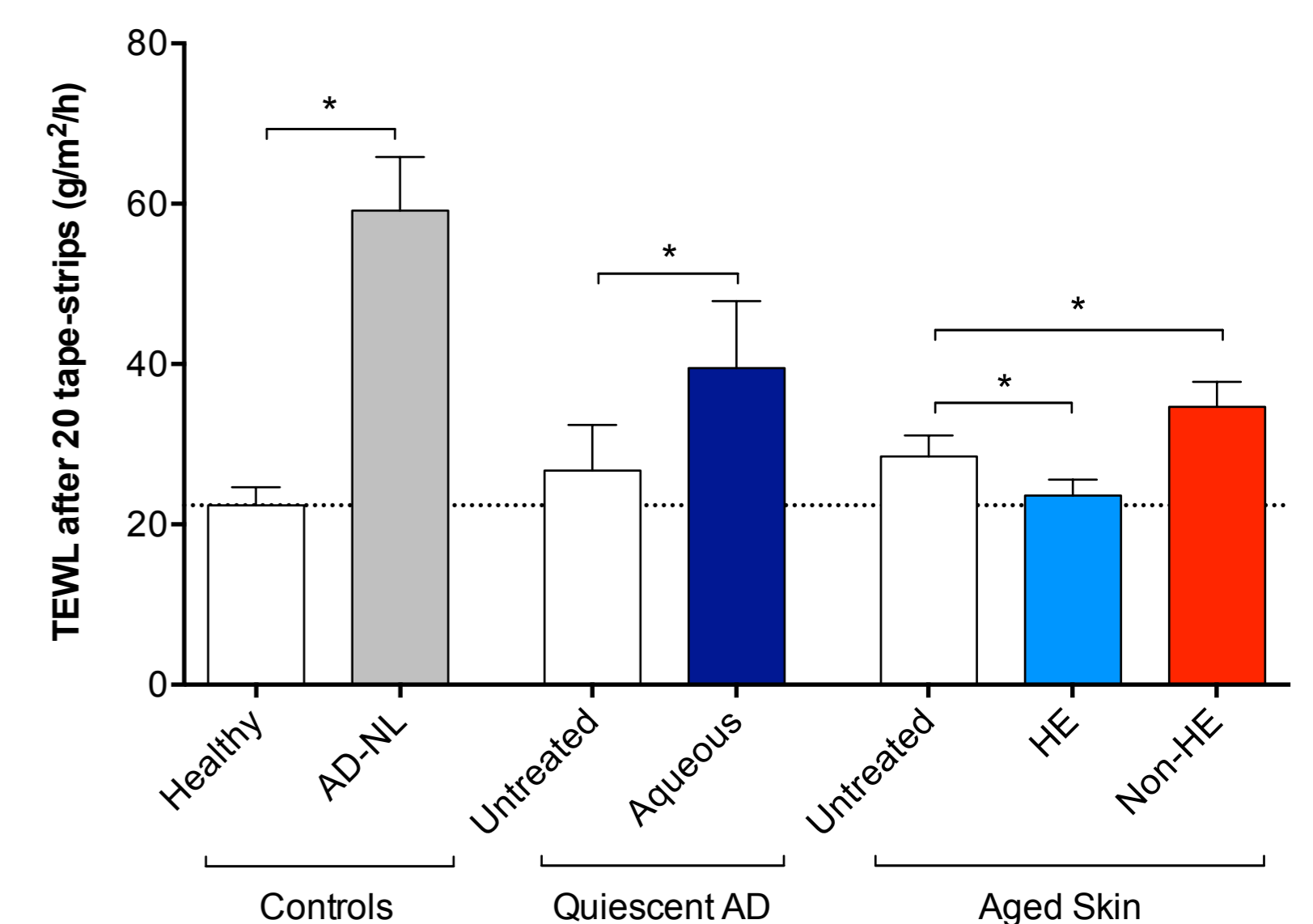


Figure 3: SC integrity before and after 28-days treatment. See Figure 2 legend for details. SC integrity was determined by measuring TEWL after experimentally damaging the skin (tape-stripping to 20 strips). If integrity is low, tape-stripping will induce more damage and the increase in TEWL will be higher.

3. Reduced SC integrity following treatment with the non-humectant emollient is associated with elevated skin-surface pH and degradatory protease activity

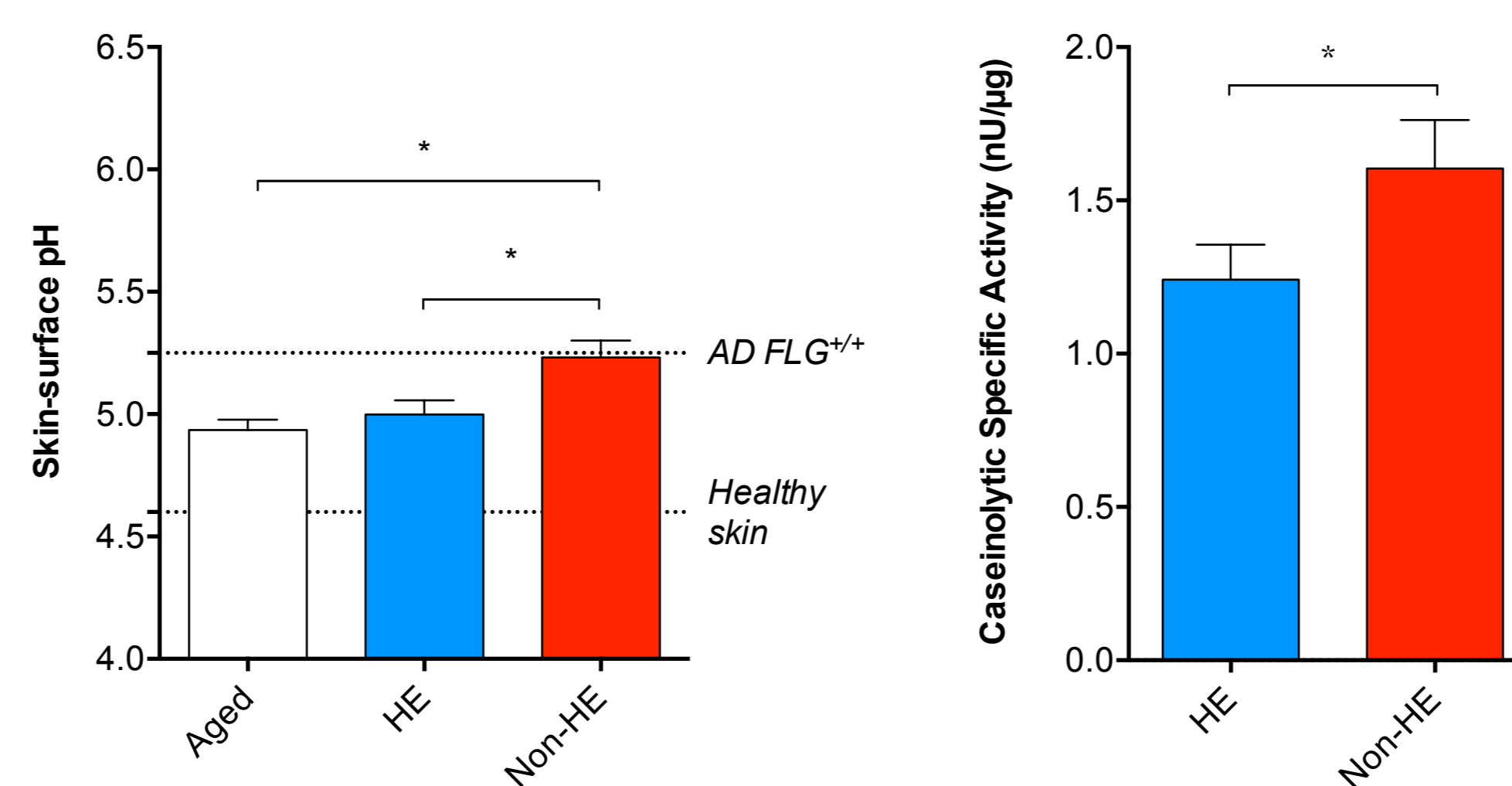


Figure 4: Skin surface pH and broad spectrum (caseinolytic) protease activity are significantly lower following 28 days treatment with the humectant emollient compared to the non-humectant emollient cream. (Left) Skin surface pH before (mean) and after treatment. *Results of a Tukey post-test shown. Dashed lines indicate skin surface pH values from Winge *et al.* 2011. (Right) Caseinolytic protease activity after treatment. *Results of a t-test shown.

4. The humectant emollient significantly hydrated the skin for more than 12 hours after cessation of treatment

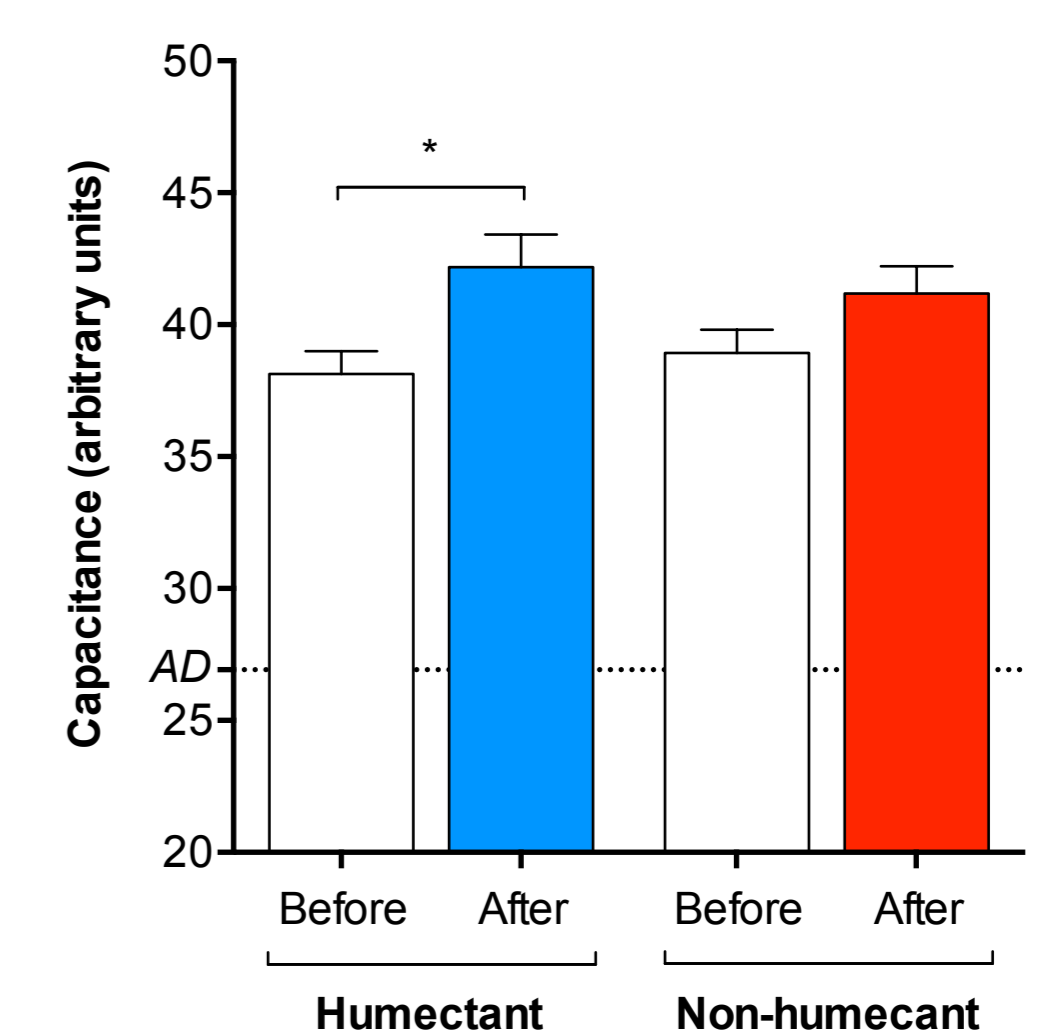


Figure 5: (Left) SC hydration before and after 28-days treatment. Measurements were taken the day after cessation of treatment (12-20 hours). *Results of a Tukey post-test shown. Dashed line indicates hydration for AD patients at non-lesional sites.

5. Treatment with the humectant emollient increases the level of water binding molecules and water in the stratum corneum

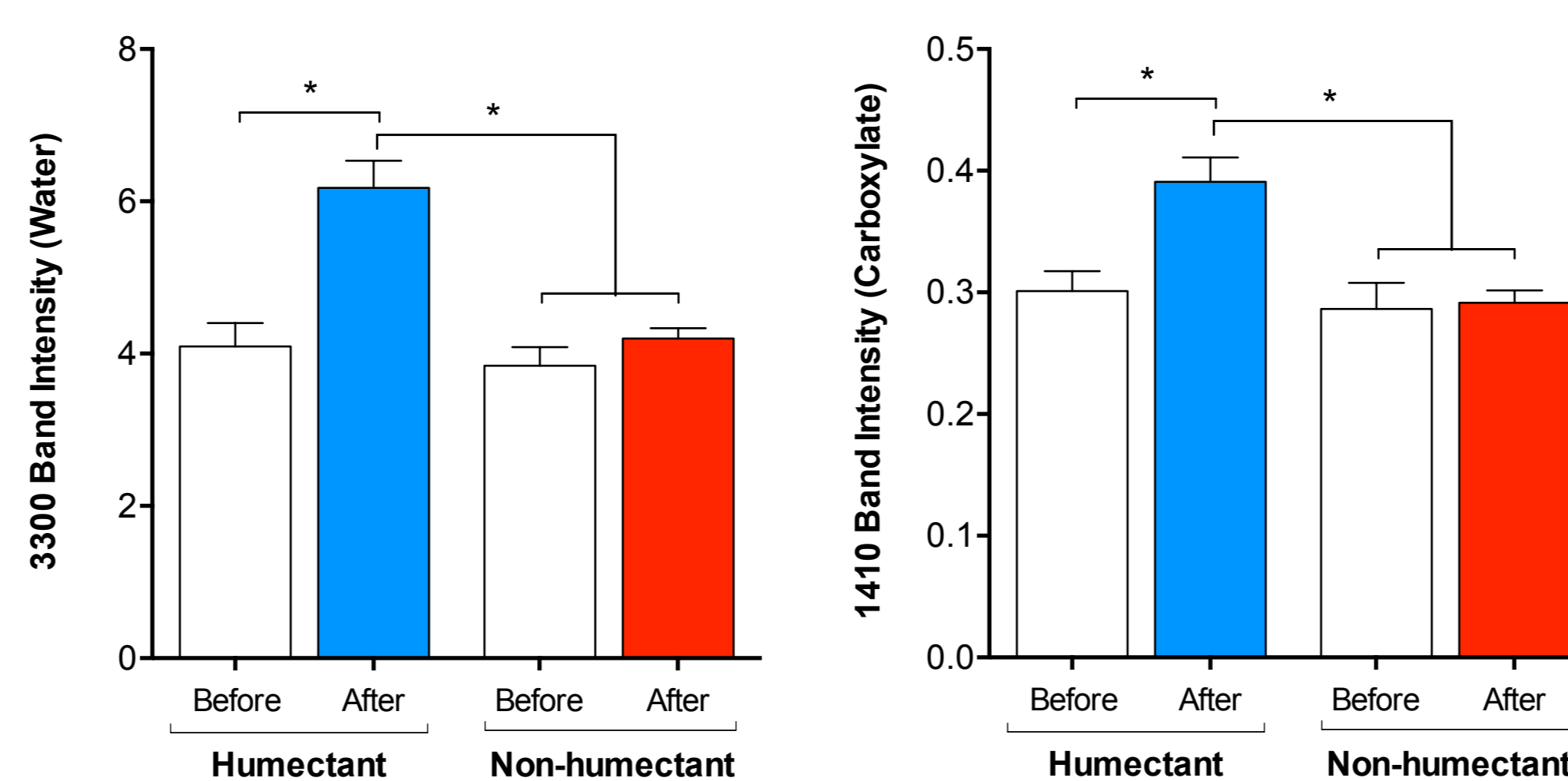


Figure 6: SC water and carboxyl group concentration before and 12-20 hours after treatment. FTIR spectra were collected after stripping the skin 3 times (removing 0.56±0.02µm) to remove surface product/water. (Left) The amount of water across the first 3.6µm SC was quantified from the intensity of the 3300 cm⁻¹ band (O-H stretching) relative to amide II (1550 cm⁻¹, N-H bending). (Right) The amount of carboxyl groups of humectants (i.e. NMF) were quantified from the intensity of the 1410 cm⁻¹ band. *Indicate the results of a Tukey post-test.

6. Treatment with the humectant emollient stimulates endogenous NMF synthesis

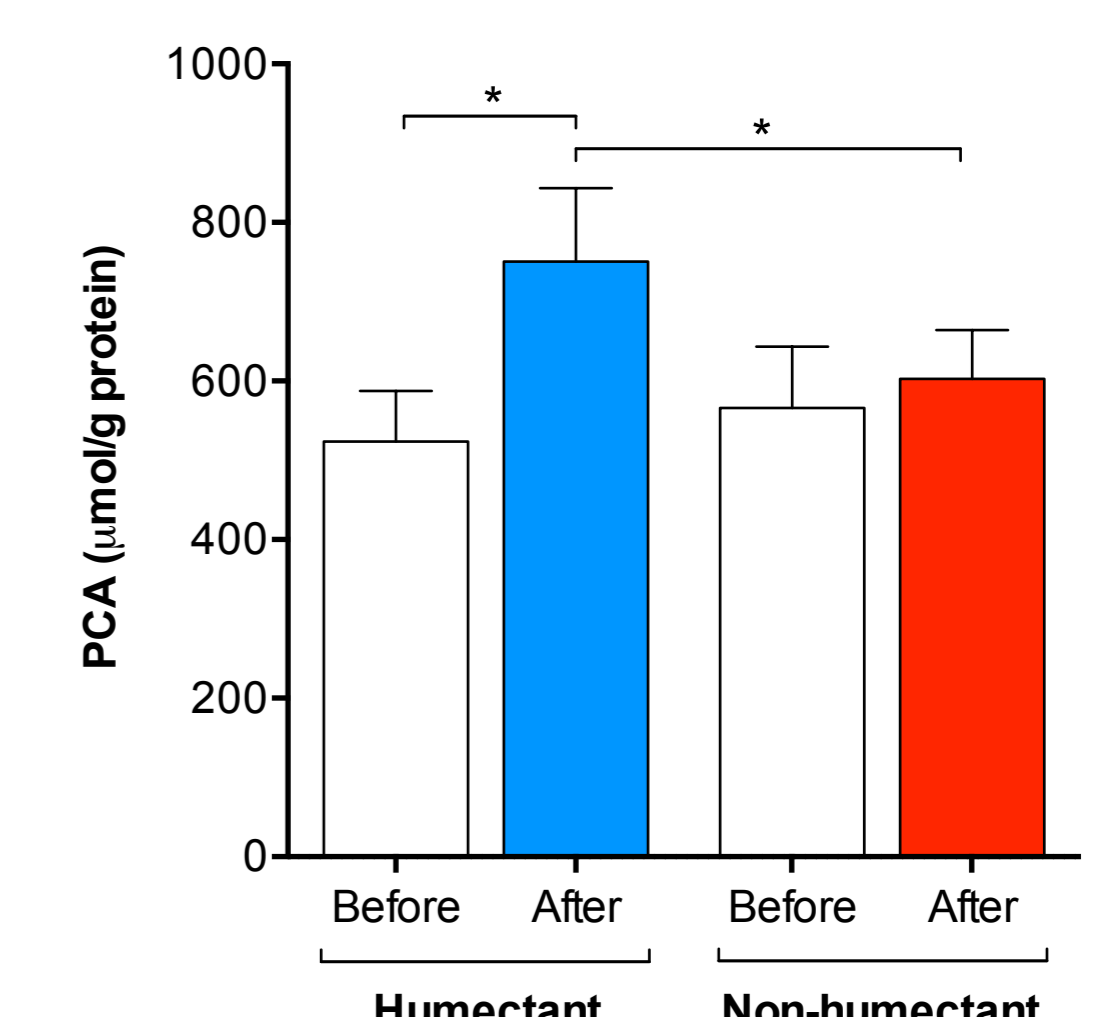


Figure 7: PCA levels in the SC were elevated following treatment with the humectant emollient (that contains no PCA), indicating increased endogenous production. Urea was recently found to stimulate filaggrin expression (and by inference NMF levels).¹³ HPLC derived PCA levels directly correlate with the amount of carboxyl groups (r 0.532, p <0.0001). *Indicate the results of a Tukey post-test.

7. The humectants in the humectant emollient penetrate the SC & increase water levels in adults with healthy skin

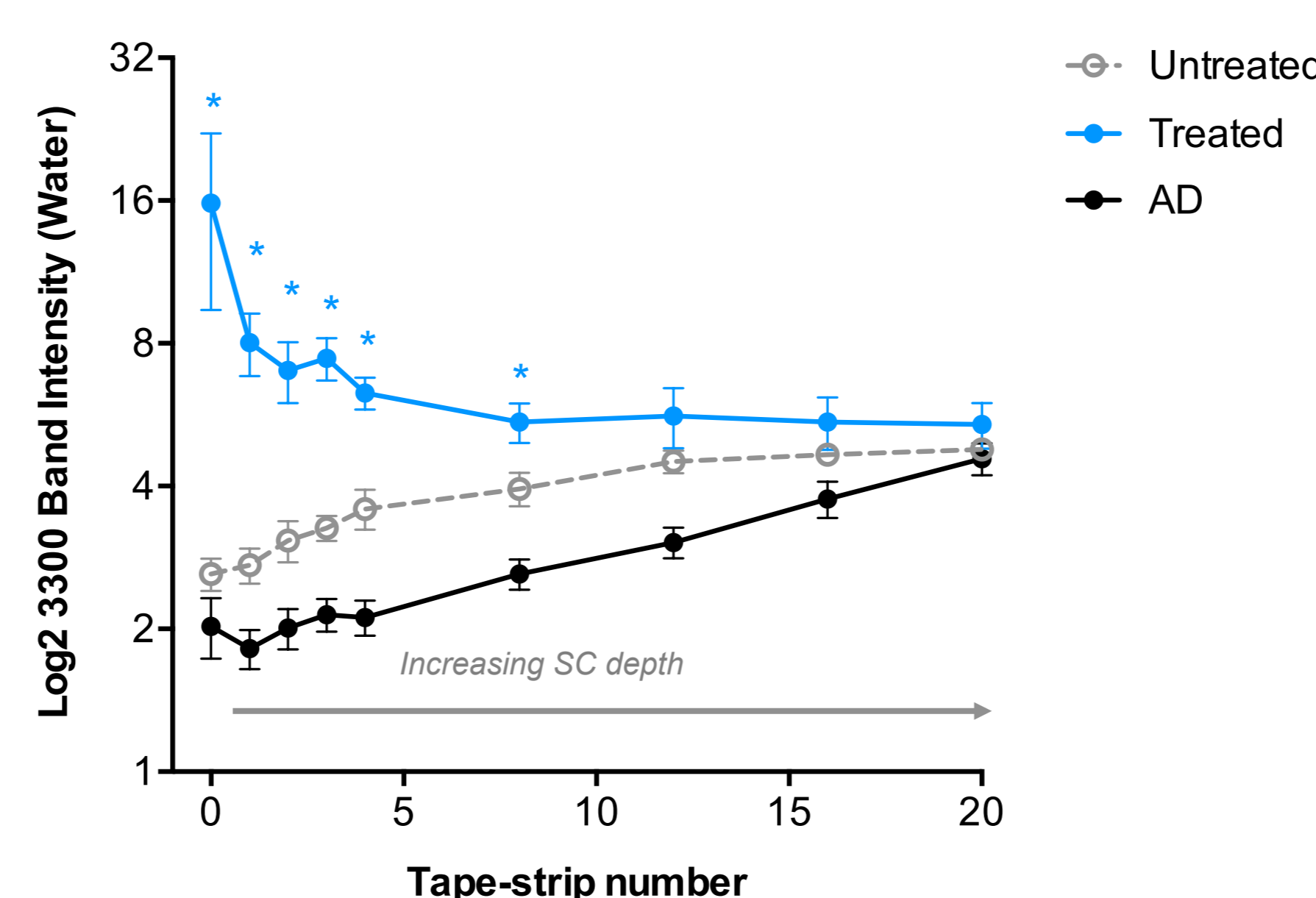


Figure 8: Water concentration (3300 cm⁻¹ relative to amide II) throughout the SC 3 hours following a single application of humectant emollient in 9 volunteers aged <60 years. Measurements at increasing SC depths were achieved by tape-stripping. FTIR penetrates 3.6µm. 5 AD patients were assessed for reference. *indicate statistical differences between treated and untreated skin.

CONCLUSIONS

- The humectant emollient significantly hydrated the skin of older people with dry skin to a greater extent and for a longer period of time compared to the non-humectant emollient.
- The humectant emollient significantly elevated SC NMF levels exogenously and endogenously, putatively via increased filaggrin expression
- Treatment with the humectant emollient for 28 days preserved skin barrier function and improved SC integrity in older people, indicative of skin barrier repair properties.
- This highlights the significant difference in effects of emollients on the skin barrier, and their potential to treat dry skin conditions.